Fast bound pool fraction quantification using stimulated echoes

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Introduction

Magnetization transfer (MT) in brain tissue is characterized commonly by a two pool proton model [1]. There is convincing evidence that the molar fraction of the protons bound to macromolecules, i.e. the bound pool fraction (*BPF*), is the pool parameter most directly linked to the composition of myelin. Recently, Schmierer et al suggested *BPF* as a predictor of myelin content in postmortem white matter [2]. *BPF* can be calculated from the pool size ratio *f* according to *BPF=f/f+1*, where *f* is defined as the ratio of macromolecular protons to free mobile water protons. Several MRI techniques for measuring *f* are available, most of them being either lengthy for whole brain coverage and/or SAR intense [3-6]. Hence, to our knowledge, none of the proposed technique has been used in clinical routine so far. To overcome these limitations, we present a fast (~5 min for 11 slices) and low SAR multislice approach which is based on a stimulated echo amplitude modulation (STEAM) preparation and a single shot echo planar imaging (sshEPI) readout. The proposed method was validated in cross-linked bovine serum albumin (BSA) probes with different concentrations and was evaluated for brain tissue in healthy volunteers.

Theory

Solving the differential equation, that describes the behavior of the longitudinal magnetization for the two pool proton model under the assumption that only the free proton pool is STEAM labeled results in a biexponential decay function of the STEAM signal S [7]. These two exponential decay terms reflect longitudinal relaxation and dilution of the STEAM labeling into the bound pool by MT (Figure 1). After TM >100ms the bound and free proton pool have approached a steady state and magnetization decays monoexponentially, thereby reducing the signal equation to $S(TM>100ms)=S_0\ 1/(f+1)\ exp(-\lambda_2 TM)$ with the MT independent relaxation rate λ_2 *and* S_0 being the net magnetization of the free proton pool before any MT has taken place. Consequently, performing STEAM experiments with minimal TM and sampling of the monoexponential decay curve allows the determination of *f* and consequently *BPF*.

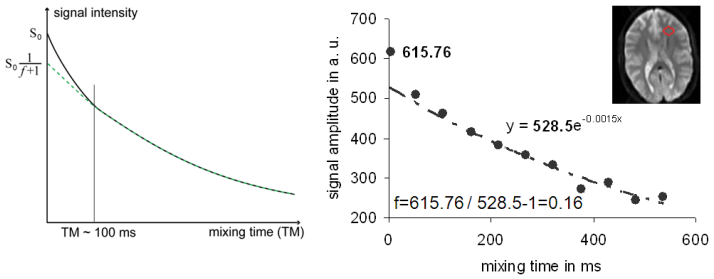

Figure 1: *Signal behavior of a STEAM experiment as a function of TM, reflecting the longitudinal magnetization of the free proton pool during TM after labeling the same one. After both proton pools reach a steady state, signal decay is monoexponential. The pool size ratio f can be calculated from the net magnetization S0 before any MT takes place and the decay rate from a monoexponential fit, as shown for frontal WM (right).*

Methods

Multislice STEAM was implemented on a 3T Tim Trio (Siemens Healthcare, Erlangen, Germany). As depicted in Figure 2, a non-slice-selective 90° pulse normalizing net magnetization for subsequent experiments is followed by a non-slice-selective preparation, with a binomial, water-only excitation pulse followed by the labeling gradient G and another rectangular 90° pulse. After shortly crushing residual transverse magnetization, a slice-selective 90° pulse flips the longitudinal magnetization for a single slice into the transversal plane before magnetization exchanges between the two pools. According to a permutation scheme minimizing crosstalk of subsequently excited slices, n slices are acquired with different TMs. A single shot EPI readout follows each excitation pulse. The experiment is repeated n times permuting the slice order such that all TMs are measured for each slice. Imaging parameters used for all data presented were: minimal TM TM0=3.2ms, TMi=(60 x i)ms+TM0, where i ranged from 1 to 10, echo time of the EPI readout TE=22ms, TR=2600ms, spatial resolution: 2.5x2.5x5mm^3, Nmax=12 slices, number of experiments Ndyn=12, NSA=5. Measurements TM2–TM10 were used for monoexponential fitting and TM0 for net magnetization before any magnetization transfer S0. The total acquisition time was 4.8min. The method was validated in six BSA phantoms with concentrations ranging from 10 to 30 % BSA to water per weight. Additionally, three healthy volunteers were scanned. f values are presented for regions of interests in the frontal WM, thalamus and caudate nucleus, which were outlined manually.

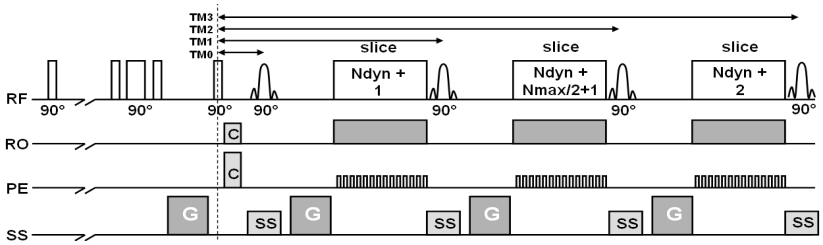

Figure 2: *Schematic of the proposed multislice STEAM sequence. Non-slice-selective water-only preparation is followed by slicewise sshEPI readout of different TMs. The slices are permuted with each experiment (Ndyn). For further details, see Methods.*

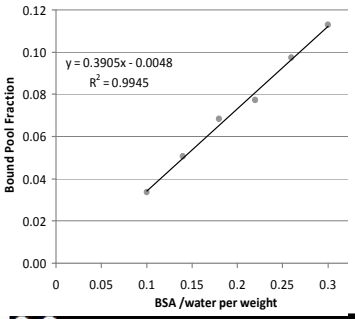

Figure 3*: Bound pool fractions (BPF= bound proton pool / (free water pool + bound proton pool)) for different concentrations of cross-linked BSA.*

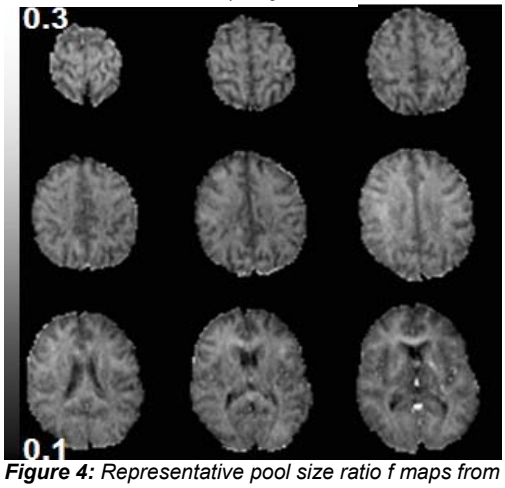

Figure 4: *Representative pool size ratio f maps from a 41-year-old healthy volunteer.*

Results

A high linearity between the BSA concentrations and measured *BPFs* was observed. Extrapolation to zero BSA concentration resulted in a negligible *BPF* offset of 0.0048 (Figure 3). Acquired *f* maps (Figure 4) provided reasonable signal to noise ratios and were highly reproducible for all volunteers. Region of interest analysis in the three healthy volunteers revealed f values ranging from 0.8-0.10, 0.14-0.15 and 0.16-0.17 for the caudate nucleus, thalamus and frontal white matter, respectively.

Discussion and Conclusion

The method proposed allows quantitative MT measurements with coverage of the entire brain within clinically feasible time. White matter values are in good agreement with literature [2-5], while deep grey matter values are slightly higher. Due to the relatively long echo time of the EPI readout the proposed method is prone to B_0 inhomogeneities and susceptibility effects. Tissue with very short transversal relaxation times exhibits very low SNR which, in turn can lead to overestimation of *f* due to fitting errors. Combination of the proposed method with acceleration strategies such as GRAPPA or SENSE promises minimization of these effects. Current work focuses on these matters.

References

[1] Henkelman et al MRM 29:759–766 (1993) [2] Schmierer et al JMRI 26(1): 41–51 (2007) [3] Yarnykh MRM 47(5):929-39. (2002) [4] Ramani et al MRM 20(10):721-31 (2002) [5] Sled et al MRM 46:923–932 (2001) [6] Gloor et al MRM 60(3):691-700 (2008) [7] Ropele et al MRM 49(5):864-71 (2003)